



Non-Pharmacological Approaches to Reducing Pain and Stress in Children During IM Injections: A Review

V. Sasireka^{1*} and G. Bhuvaneswari²

¹Child Health Nursing, Saveetha College of Nursing, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

²Department of Community Health Nursing, Saveetha College of Nursing, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India

Author Designation: ¹PhD Scholar, ²Professor

*Corresponding author: V. Sasireka (e-mail: sasireka82@yahoo.com).

©2025 the Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>)

Abstract Effective pain and stress management during pediatric intramuscular injections is essential, particularly for neonates and young children, who are more sensitive due to developmental factors. This review highlights Non-Pharmacological Interventions (NPIs) designed to reduce procedural pain and distress in children from neonates to adolescents. Preterm neonates are especially vulnerable as their immature neuroregulatory pathways can lead to long-term neurodevelopmental issues if pain is not managed properly. Pediatric intramuscular injections can cause both physiological stress responses and psychological distress, potentially contributing to needle fear and avoidance of healthcare in the future. NPIs such as distraction techniques (e.g., distraction cards, cold-vibration devices and virtual reality), caregiver involvement, comfort positioning and complementary therapies like breastfeeding and oral sucrose have been proven to be safe and effective. These interventions help reduce pain intensity, behavioral distress and physiological stress markers without the side effects of pharmacological treatments. However, gaps remain in understanding the best NPI combinations for different developmental stages, their long-term effects and their use in specific neonatal procedures, such as endotracheal suctioning. Integrating evidence-based NPIs aligns with the principles of atraumatic care, enhancing children's procedural experiences and building trust between healthcare providers, caregivers and patients. To optimize pain management across pediatric populations, future research should focus on age-specific protocols, the use of emerging digital technologies and personalized, multimodal strategies for sustainable pain management. Large-scale studies are needed to explore these aspects further and to refine approaches for pain management in pediatric care.

Key Words Pain, Stress, Non pharmacological, Intramuscular Injection

INTRODUCTION

Neonates, especially those born prematurely, show a heightened sensitivity to painful stimuli when compared to older children. This vulnerability is largely due to the fact that ascending pain pathways, capable of transmitting noxious impulses, are already functional by 24 weeks of gestation, whereas the neurotransmitters that regulate and modulate these impulses do not mature until around 48 weeks [1,2]. Because of this imbalance, repeated exposure to painful events at such a critical stage can alter neuronal and synaptic development in lasting ways. The cerebral cortex is particularly susceptible to these effects, as pain not only damages neurons directly but also modify the stress-response systems of the body. When pain is not adequately treated, premature infants are left more vulnerable to adverse

clinical and behavioral outcomes later in life [1]. Both human studies and animal models support the idea that the immature nervous system is highly reactive to tactile and noxious stimulation. In newborns, even routine procedures such as heel pricks trigger strong spinal reflexes and measurable nociceptive activity in the brain [3-5]. Younger infants, in particular, demonstrate more prolonged responses to such painful events [6]. With major advances in neonatal care, the survival rates of extremely premature and critically ill infants have greatly improved [7]. However, these improvements have also highlighted the long-term risks of survival, as many infants go on to develop cerebral palsy, sensory impairments, learning difficulties and respiratory complications [7,8]. A significant concern in neonatal intensive care is the exposure of preterm infants to

repeated painful interventions during a period of rapid brain growth, active synaptogenesis and receptor maturation [9-11]. For example, nearly two-thirds of infants born before 29 weeks' gestation require mechanical ventilation [12]. Such infants are often intubated and undergo repeated suctioning of the airway. Endotracheal suctioning has been identified as one of the most frequent and most painful procedures in the NICU setting, with effects ranging from moderate to severe pain [13,14]. Even when performed using standardized nursing techniques, this procedure still causes discomfort in premature infants [15].

Reliable and valid assessment of pain in neonates is essential, yet despite the availability of multiple tools, neonatal pain is still frequently under-recognized and under-treated [16,17]. Effective management is crucial not only to minimize immediate distress but also to protect the developing nervous system from long-term alterations in pain processing. By preventing persistent sensitization of neural pathways, appropriate interventions can help safeguard central nervous system development and overall neurodevelopmental outcomes [17]. One of the simplest ways to reduce pain caused by suctioning is to minimize the frequency of the procedure. Alongside this, a wide range of non-pharmacological strategies has been developed to reduce neonatal stress during painful events [18]. These include the use of sucrose or breast milk, non-nutritive sucking, skin-to-skin contact, facilitated tucking, swaddling, cuddling, rocking, massage, exposure to familiar odors, video distraction and environmental modifications designed to support development [19]. Evidence shows that these interventions can lessen both behavioral and physiological indicators of pain, while also improving parent and caregiver satisfaction [20].

Research indicates that non-pharmacological approaches are effective in alleviating pain from procedures such as venipuncture, heel pricks and intramuscular injections. They appear to work best when used in combination rather than individually and importantly, no serious adverse effects have been reported in association with their use [21,19]. Skin-to-skin care, often referred to as kangaroo care, has been shown to reduce pain responses safely without complications [22]. Similarly, facilitated tucking and swaddling help maintain physiological and behavioral stability, reducing crying time and supporting better regulation of sleep and motor activity [23,24]. Non-nutritive sucking, whether using a pacifier or a gloved finger, has also been shown to regulate discomfort, reduce pain duration and improve oxygenation and gastrointestinal function, again without reported side effects [23,24]. The use of oral sucrose has been widely studied and found effective in reducing pain behaviors during procedures such as venipuncture and injections. While it does not appear to reduce the direct nociceptive activity recorded in the brain, sucrose clearly reduces observable distress behaviors such as crying [25,26]. Small doses of 24% sucrose have been sufficient to reduce pain in preterm infants, although the most effective dose and long-term safety of repeated

administration are still under investigation [26]. Other methods such as gentle rocking, massage, exposure to familiar odors and video distraction also show promise, though more high-quality research is needed [19].

More specialized interventions, such as acupuncture and Transcutaneous Electrical Nerve Stimulation (TENS), have been explored in neonatal settings as well. These methods activate endogenous pain inhibitory pathways and have been widely accepted for use in adults. However, their effectiveness in neonates remains inconsistent, with some studies suggesting benefits while others show no significant reduction in pain during procedures like heel pricks [27]. Multisensory stimulation combining auditory, tactile, gustatory, vestibular and visual inputs has also been tried but its benefits appear limited and in some cases, it may overstimulate the preterm infant [28-31]. Despite several reviews highlighting the value of non-pharmacological strategies in neonatal pain management [32-35], their specific application during endotracheal suctioning remains underexplored. Given the frequency and painful nature of this procedure, it is essential to identify which strategies are most effective in this context. Although adherence to pain management guidelines has improved, many neonates still experience undertreated pain in NICUs. Clinicians and researchers therefore have a responsibility to reduce exposure to painful stimuli, while implementing effective, evidence-based interventions that protect neurodevelopment. Repeated exposure to uncontrolled pain in both term and preterm neonates has lasting consequences, affecting pain sensitivity later in life as well as impairing cognition, motor development and overall brain growth [36-39]. For this reason, neonatal pain management must be prioritized as an essential aspect of neuroprotection. By minimizing invasive stressors, carefully monitoring pain and adopting individualized care strategies, healthcare providers can significantly reduce abnormal sensory input and stress, thereby supporting healthier neuronal development and synaptogenesis in these vulnerable infants [40,41].

Non-pharmacological interventions (NPIs) play a critical role in reducing pain and stress in children undergoing intramuscular (IM) injections, particularly given the potential for long-term consequences such as needle fear and healthcare avoidance. Interventions such as distraction techniques, caregiver involvement and comfort positioning have demonstrated effectiveness in minimizing pain and distress without the adverse effects associated with pharmacological treatments. However, research gaps persist regarding the optimal combinations of NPIs for different developmental stages and their long-term efficacy. There is also a lack of standardized protocols for NPI implementation and limited research on the barriers to their consistent use in clinical practice. Addressing these gaps is essential to develop personalized, multimodal strategies that enhance pain management and improve the overall quality of pediatric care during medical procedures. The aim of this review is to evaluate the effectiveness, safety and feasibility

of non-pharmacological approaches for reducing pain and stress in children during intramuscular injections.

METHODS

This narrative review involved a comprehensive search of several electronic databases, including PubMed, CINAHL and Scopus, to identify relevant studies on non-pharmacological approaches to reducing pain and stress during pediatric intramuscular injections. The inclusion criteria comprised peer-reviewed articles published between 2010 and 2025, focusing on NPIs used in children of all pediatric age groups, from neonates to adolescents. Studies were selected based on their relevance to the topic, methodological quality and clear reporting of outcomes related to pain intensity, stress reduction or behavioral distress. Both experimental and observational studies were included, along with systematic reviews and clinical guidelines. Articles not published in English or those focused solely on pharmacological interventions were excluded. This review synthesizes the findings from the selected studies to provide an overview of effective non-pharmacological interventions for pediatric injection-related pain and stress.

Physiological and Psychological Stress During IM Injections

Children experience pain differently from adults because of their developmental stage and limited ability to rationalize medical procedures. Injections are often perceived as threatening events, which amplifies pain and distress, especially when combined with anticipatory anxiety before the procedure begins [42]. Physiologically, IM injections activate both the sympathetic nervous system and the Hypothalamic-Pituitary-Adrenal (HPA) axis, leading to measurable changes such as increased heart rate, elevated blood pressure, rapid breathing and alterations in autonomic activity like sweating and facial flushing. Endocrine responses are also evident, with salivary cortisol levels shown to rise significantly in children undergoing painful medical procedures, confirming their stress response [43]. Alongside these physiological effects, IM injections can cause important psychological sequelae. Children frequently exhibit fear, crying and avoidance behaviors and repeated negative experiences may create conditioned responses in which simply seeing a syringe or entering a clinic environment provokes anxiety [44]. Such experiences can erode trust in healthcare providers and foster long-term negative associations with medical care, leading to avoidance of essential preventive procedures such as vaccinations [45]. If pain and stress are not properly managed, these early adverse experiences can contribute to needle phobia in adolescence and adulthood, reduce adherence to medical care and negatively shape coping mechanisms later in life [46].

Non-Pharmacological Approaches

Non-Pharmacological Interventions (NPIs) are a range of strategies designed to alleviate pain and distress without

using medications. These approaches focus on modulating attention, sensory input and emotional environment, often utilizing caregiver presence to enhance comfort. In pediatric care, intramuscular (IM) injections are common but anxiety-inducing, with children frequently experiencing both acute pain and anticipatory stress. NPIs aim to distract attention from the needle, provide alternative sensory stimulation or offer reassurance through caregiver involvement. Because they do not rely on pharmacological agents, NPIs eliminate the risk of drug-related side effects and are easily applicable across diverse pediatric populations. They are particularly beneficial in high-throughput settings such as immunization clinics and hospital wards, where efficient, safe and effective pain management is crucial [47]. Clinical evidence supports the significant impact of NPIs. Systematic reviews consistently show that strategies like distraction, caregiver participation, proper positioning and sensory adjuncts not only reduce self-reported pain but also decrease observable behavioral distress, including crying, withdrawal and agitation. Some NPIs also reduce physiological stress responses, with documented effects on heart rate, blood pressure and cortisol levels [43]. Additionally, NPIs help prevent long-term negative healthcare associations, such as needle phobia or vaccine avoidance. By incorporating NPIs into routine practice, healthcare professionals can align with atraumatic care principles, build trust between children and caregivers and improve the overall quality and experience of pediatric care (Figure 1).

Distraction Methods for Reducing Pain and Anxiety During Intramuscular Injections in Children

Distraction techniques have proven to be an effective non-pharmacological intervention for reducing pain and anxiety during pediatric intramuscular (IM) injections. From a neurophysiological standpoint, these strategies function through attentional modulation and sensory gating, limiting the processing of nociceptive signals. Cold-vibration devices, like Buzzy®, activate large-diameter A-β fibers to inhibit pain transmission via gate-control mechanisms, offering strong evidence of efficacy in reducing pain during needle procedures, particularly in older children with better attentional control [48,50]. Distraction cards, a low-cost intervention, have shown significant reductions in pain and anxiety in children aged 6-11 years undergoing IM injections [49]. Additionally, immersive technologies such as Virtual Reality (VR) have demonstrated substantial benefits in reducing pain and anxiety. In a multicenter RCT, VR distraction significantly lowered pain and behavioral distress in children undergoing venipuncture [52]. Similarly, VR reduced anxiety and pain in dental procedures compared to traditional screen-based distractions [53]. Simple distraction methods, like bubble-blowing, have also proven effective in reducing pain and fear, especially in primary care settings [54]. The combined evidence highlights the effectiveness of both traditional and advanced distraction interventions, with immersive and device-based methods showing superior efficacy in certain contexts. Future research should focus on head-to-head comparisons of these techniques during IM

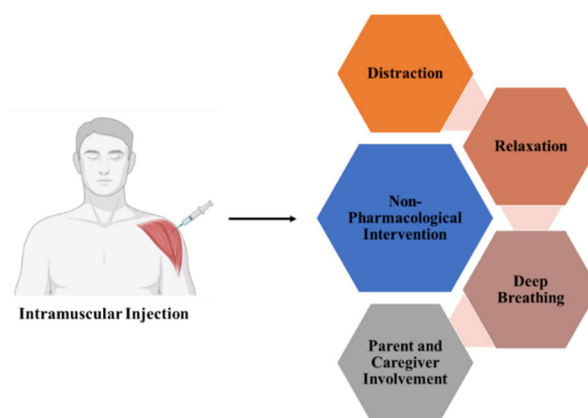


Figure 1: Non-Pharmacological Interventions for Intramuscular Injection Pain Management in Children

Table 1: Distraction Methods for Needle-Related and IM Injection Pain in Children

Distraction Method	Age Group (years)	Design and Sample Size	Pain/Anxiety Outcomes	Reference
Distraction cards	6-11	RCT; n = 60	Lower self-, parent- and observer-reported pain; reduced parent/observer anxiety	Czub <i>et al.</i> [49]
Buzzy vs. Shot Blocker vs. bubble-blowing	5-10	RCT; n = 120	Buzzy® superior in reducing pain and fear vs. Shot Blocker and bubble-blowing	Northington [51]
Virtual reality (VR)	5-9	Multicenter RCT; n = 304	VR significantly reduced pain, anxiety and distress compared with standard care	Prabhakar <i>et al.</i> [52]
VR vs. cartoon video	6-12	RCT; n = 90	VR yielded significantly lower pain and anxiety than 2D cartoons	Simpson and Knox [54]
Bubble-blowing/touch	4-6	RCT; n = 45	Both techniques reduced pain perception and fear	Chambers <i>et al.</i> [55]
Audiovisual glasses	5-7	Split-mouth trial; n = 30	Watching cartoons via A/V glasses reduced pain compared with no distraction	Felemban <i>et al.</i> [53]

injections, age-related factors and long-term outcomes such as reduced needle fear and improved healthcare adherence [55]. Future studies should prioritize head-to-head trials of distraction modalities specifically during IM injections, explore age-related moderators and examine long-term outcomes such as reduced needle fear and improved healthcare adherence.

Finding from Reviewed Studies

The studies included in Table 1 show a range of methodologies, with several Randomized Controlled Trials (RCTs) and a meta-analysis, providing robust evidence for the effectiveness of distraction techniques in reducing pain and anxiety in children, though variability in sample sizes and methods exists.

Parent and Caregiver Involvement

Parental and caregiver involvement is increasingly recognized as a critical component in pediatric pain management during intramuscular (IM) injections. Children often rely on their caregivers for comfort and security during medical procedures and the presence of a trusted parent can significantly reduce procedural distress, enhance coping strategies and improve both immediate and long-term emotional responses to pain [56]. The behavior of caregivers plays a pivotal role in shaping these outcomes. Calm, supportive and reassuring caregivers foster a sense of safety, while anxious or distressed responses can heighten the child's perception of pain [57]. Research has shown that

children whose parents model adaptive coping behaviors, such as using distraction techniques or providing positive verbal reassurance, report significantly lower pain scores and exhibit reduced behavioral distress.

Caregiver involvement also influences physiological responses. Birnie *et al.* [58] demonstrated that parental support combined with distraction methods like storytelling, singing or playing with electronic devices led to greater reductions in heart rate and pain intensity compared to distraction alone. This highlights the added value of combining caregiver involvement with other non-pharmacological interventions. Furthermore, training caregivers prior to procedures has been shown to improve outcomes. Educational interventions that teach parents anxiety-management techniques and strategies to support their children lead to better results during IM injections [59]. Prepared parents are more likely to stay calm, provide consistent reassurance and engage in effective distraction activities, which optimizes the child's experience and empowers the caregiver. Overall, caregiver involvement is not just supplementary but essential to effective pain management, transforming potentially traumatic events into more manageable experiences [60].

Positioning and Environmental Modifications

In addition to caregiver involvement, physical positioning and environmental factors significantly influence how children experience IM injections. Traditional practices, such as restraining children in the supine position, are

Increasingly discouraged due to their association with heightened fear, distress and negative medical memories [61]. Comfort positioning, which includes holding the child in a caregiver's lap, supporting an upright seated posture or using gentle physical containment, has been linked to lower distress behaviors, reduced crying and improved cooperation during procedures [62]. The rationale behind comfort positioning is multifaceted; upright positions provide children with a greater sense of control, reduce the perceived threat of being overpowered and facilitate eye contact with caregivers, offering reassurance [61]. Additionally, close physical proximity to caregivers may trigger oxytocin release and other neurobiological mechanisms that buffer the stress response and reduce pain perception.

Tactile modifications, such as gentle stroking or applying pressure near the injection site, can also decrease pain, likely through the activation of competing sensory pathways, as described by the gate control theory of pain. These strategies are simple, inexpensive and do not require specialized equipment, making them ideal for pediatric practice. Environmental factors also play a crucial role in reducing distress. Child-friendly environments with colorful murals, interactive toys and distraction elements such as music or cartoons have been shown to lower anticipatory anxiety before injections [62]. In contrast, sterile, medical environments can heighten vigilance and distress. Interventions like minimizing visible medical tools, shortening waiting times and incorporating playful elements can further enhance the child's experience. When combined, comfort positioning and environmental modifications produce additive benefits, reducing both fear and pain during injections [58]. These strategies are low-cost and feasible for implementation in both high- and low-resource healthcare settings. Collectively, they show that children's pain during IM injections is not just a biological response but a biopsychosocial experience shaped by caregiver involvement, positioning and environment. Integrating these evidence-based strategies into routine practice can significantly improve pediatric procedural care, minimizing trauma and promoting positive healthcare experiences [63].

The comparative analysis of Non-Pharmacological Interventions (NPIs) highlights how strategies for pain

and stress management during intramuscular (IM) injections must be tailored to the developmental stage of the child. In infants, breastfeeding, sucrose and non-nutritive sucking consistently provide effective analgesia by combining sensory stimulation, taste-mediated endogenous opioid release and caregiver contact. These approaches not only reduce crying and behavioral distress but also lower physiological stress responses, making them highly practical for immunization settings in Table 2 [43].

In preschool and school-age children, distraction techniques and comfort positioning are central to effective pain management. Simple tools such as distraction cards, bubbles and toys successfully redirect attention, while upright positioning and caregiver presence foster a sense of security and control. Evidence demonstrates that as children's cognitive capacities mature, more sophisticated distraction strategies become feasible. For school-aged children, devices like Buzzy® and Shot Blocker® leverage cold and vibration to activate the gate-control mechanism, while interactive media such as cartoons, tablets and video games further sustain attention and reduce anticipatory anxiety [44]. Among adolescents, NPIs that emphasize autonomy and cognitive engagement, such as virtual reality, guided imagery and self-directed distraction, show the greatest promise. These interventions empower adolescents to actively manage their pain perception, reduce anxiety and improve cooperation during procedures. Importantly, across all age groups, the involvement of caregivers, supportive positioning and child-friendly environments serve as universal enhancers of intervention effectiveness. Systematic reviews confirm that these strategies significantly reduce behavioral distress, self-reported pain and physiological stress responses, demonstrating the robustness and versatility of NPIs in pediatric clinical practice [43].

Complementary Therapies

Complementary therapies provide additional strategies for reducing pain and anxiety during pediatric intramuscular (IM) injections. Cold-vibration devices like Buzzy® leverage the gate-control theory of pain, combining vibration and cold to inhibit nociceptive signals,

Table 2: Age-Specific Non-Pharmacological Interventions for Pain and Stress Reduction during IM Injections

Age Group	Most Effective NPIs	Mechanism/Benefit	References
Infants (<1 year)	Breastfeeding-Oral sucrose/glucose-Non-nutritive sucking	Sweet taste triggers endogenous opioid release; skin-to-skin contact enhances comfort; sucking reduces stress and crying.	Northington [51]
Preschool Children (1-5 years)	Distraction with toys, bubbles, cartoons-Comfort positioning (upright sitting, caregiver holding)	Engages attention away from pain; upright positions reduce perceived threat; parental presence lowers anxiety.	Taddio <i>et al.</i> [43], Canbulat and Türkmen [48]
School-Age Children (6-12 years)	Distraction cards-Cold & vibration devices (Buzzy®, ShotBlocker®)-Multimedia (cartoons, tablets, video games)	Activates competing Sensory/cognitive pathways; vibration & cold block nociceptive transmission (gate control); multimedia maintains sustained engagement.	Yilmaz and Alemdar [44], Inal and Kelleci [50]
Adolescents (13-18 years)	Virtual reality (VR)-Guided imagery-Deep breathing & self-directed distraction	Enhances sense of control; immersive environments reduce pain salience; relaxation lowers physiological stress responses.	Inal and Kelleci [50]
Across All Age Groups	Parental presence & reassurance-Child-friendly environment (colors, murals, play areas)-Positioning (upright vs. supine)	Emotional support reduces fear; enriched environments reduce anticipatory stress; positioning increases comfort and cooperation.	Taddio <i>et al.</i> [43], Inal and Kelleci [50]

significantly reducing pain and fear during injections and outperforming other distraction techniques like Shot Blocker® and bubble-blowing [44]. For infants, breastfeeding during vaccinations is highly effective due to the combined benefits of sweet taste, skin-to-skin contact and warmth, while oral sucrose and non-nutritive sucking serve as effective alternatives when breastfeeding is not possible [65].

Acupressure, which applies manual pressure to specific acupoints, has been shown to reduce procedural pain in children undergoing needle-related procedures, suggesting its potential for IM injections [66]. Aromatherapy, particularly with essential oils like orange and lavender, has demonstrated anxiety-reducing effects in pediatric settings, making it a promising adjunct to reduce anticipatory anxiety, especially in waiting areas [67]. These complementary therapies provide versatile, age-appropriate options to enhance pediatric pain management and improve procedural experiences.

CONCLUSIONS

Non-Pharmacological Interventions (NPIs) such as distraction methods, caregiver involvement, comfort positioning and complementary therapies like cold vibration and breastfeeding effectively reduce pain, behavioral distress and physiological stress during pediatric intramuscular injections. These strategies not only improve the immediate procedural experience but also foster long-term trust in healthcare systems and support atraumatic care principles. Integrating NPIs into routine pediatric practice enhances care quality, minimizes negative healthcare associations and empowers children and families. Future research should focus on optimizing NPI combinations across age groups and clinical settings to further improve pain management and patient-provider relationships.

Recommendations

It is recommended that healthcare providers integrate Non-Pharmacological Interventions (NPIs) such as cold-vibration devices, caregiver involvement and comfort positioning to effectively manage pediatric pain and anxiety during IM injections. Additionally, incorporating complementary therapies like breastfeeding, acupressure and aromatherapy can enhance pain relief and reduce stress.

Limitations and Future Directions

While Non-Pharmacological Interventions (NPIs) show strong evidence for reducing pain and distress during intramuscular injections, several limitations exist. Differences in age, temperament and cultural context can influence children's responses, making it difficult to generalize findings across diverse populations [67]. Most studies emphasize short-term outcomes such as immediate pain and crying, with little data on long-term effects like reducing future needle phobia or improving attitudes toward healthcare. Additionally, many trials are limited by small sample sizes and lack of direct comparisons between multiple NPIs, highlighting the need for large-scale, multicenter randomized controlled trials to establish standardized guidelines. Future research should also evaluate the

feasibility and scalability of newer technologies such as mobile apps and virtual reality, particularly in low-resource settings and explore hybrid, multimodal approaches that combine distraction, caregiver involvement and sensory modulation for more personalized and sustainable pain management strategies [68].

REFERENCES

- [1] Anand, K.J. *et al.* "Analgesia and Sedation in Preterm Neonates Who Require Ventilatory Support: Results from the NOPAIN Trial." *Archives of Pediatrics & Adolescent Medicine*, vol. 153, no. 4, 1999, pp. 331-338. <https://doi.org/10.1001/archpedi.153.4.331>.
- [2] Hatfield, L.A. "Neonatal Pain: What's Age Got to Do with It?" *Surgical Neurology International*, vol. 5, suppl. 13, 2014, pp. S479-S489. <https://doi.org/10.4103/2152-7806.144630>.
- [3] Cornelissen, L. *et al.* "Postnatal Temporal, Spatial and Modality Tuning of Nociceptive Cutaneous Flexion Reflexes in Human Infants." *PLoS One*, vol. 8, no. 10, 2013, e76470. <https://doi.org/10.1371/journal.pone.0076470>.
- [4] Fabrizi, L. *et al.* "A Shift in Sensory Processing That Enables the Developing Human Brain to Discriminate Touch from Pain." *Current Biology*, vol. 21, no. 18, 2011, pp. 1552-1558. <https://doi.org/10.1016/j.cub.2011.08.010>.
- [5] Slater, R. *et al.* "Evoked Potentials Generated by Noxious Stimulation in the Human Infant Brain." *European Journal of Pain*, vol. 14, no. 3, 2010, pp. 321-326. <https://doi.org/10.1016/j.ejpain.2009.05.005>.
- [6] Fitzgerald, M. and S. Gibson. "The Postnatal Physiological and Neurochemical Development of Peripheral Sensory C Fibres." *Neuroscience*, vol. 13, no. 3, 1984, pp. 933-944. [https://doi.org/10.1016/0306-4522\(84\)90107-6](https://doi.org/10.1016/0306-4522(84)90107-6).
- [7] Glass, H.C. *et al.* "Outcomes for Extremely Premature Infants." *Anesthesia & Analgesia*, vol. 120, no. 6, 2015, pp. 1337-1351. <https://doi.org/10.1213/ANE.0000000000000705>.
- [8] Younge, N. *et al.* "Survival and Neurodevelopmental Outcomes among Periviable Infants." *The New England Journal of Medicine*, vol. 376, no. 7, 2017, pp. 617-628. <https://doi.org/10.1056/NEJMoa1605566>.
- [9] Anand, K.J.S. "Effects of Perinatal Pain and Stress." *Progress in Brain Research*, vol. 122, 2000, pp. 117-129. [https://doi.org/10.1016/s0079-6123\(08\)62134-2](https://doi.org/10.1016/s0079-6123(08)62134-2).
- [10] Bhutta, A.T. and K.J.S. Anand. "Vulnerability of the Developing Brain: Neuronal Mechanisms." *Clinics in Perinatology*, vol. 29, no. 3, 2002, pp. 357-372. [https://doi.org/10.1016/s0095-5108\(02\)00011-8](https://doi.org/10.1016/s0095-5108(02)00011-8).
- [11] Brummelte, S. *et al.* "Procedural Pain and Brain Development in Premature Newborns." *Annals of Neurology*, vol. 71, no. 3, 2012, pp. 385-396. <https://doi.org/10.1002/ana.22267>.
- [12] Giaccone, A. *et al.* "Definitions of Extubation Success in Very Premature Infants: A Systematic Review." *Archives of Disease in Childhood-Fetal and Neonatal Edition*, vol. 99, no. 2, 2014, pp. F124-F127. <https://doi.org/10.1136/archdischild-2013-304896>.
- [13] Cignacco, E. *et al.* "Neonatal Procedural Pain Exposure and Pain Management in Ventilated Preterm Infants during the First 14 Days of Life." *Swiss Medical Weekly*, vol. 139, no. 15-16, 2009, pp. 226-232. <https://doi.org/10.4414/smww.2009.12545>.
- [14] Hadian, Z.S. and R.S. Sabet. "The Effect of Endotracheal Tube Suctioning Education of Nurses on Decreasing Pain in Premature Neonates." *Iranian Journal of Pediatrics*, vol. 23, no. 3, 2013, pp. 340-344.

- [15] Ward-Larson, C. *et al.* "The Efficacy of Facilitated Tucking for Relieving Procedural Pain of Endotracheal Suctioning in Very Low Birthweight Infants." *MCN: The American Journal of Maternal/Child Nursing*, vol. 29, no. 3, 2004, pp. 151-158. <https://doi.org/10.1097/00005721-200405000-00004>.
- [16] Manworren, R.C. and J. Stinson. "Pediatric Pain Measurement, Assessment, and Evaluation." *Seminars in Pediatric Neurology*, vol. 23, no. 3, 2016, pp. 189-200. <https://doi.org/10.1016/j.spen.2016.10.001>.
- [17] Walker, S.M. "Neonatal Pain." *Pediatric Anesthesia*, vol. 24, no. 1, 2014, pp. 39-48. <https://doi.org/10.1111/pan.12293>.
- [18] Attarian, S. *et al.* "The Neurodevelopmental Impact of Neonatal Morphine Administration." *Brain Sciences*, vol. 4, no. 2, 2014, pp. 321-334. Doi:10.3390/brainsci4020321.
- [19] Pillai Riddell, R.R. *et al.* "Non-Pharmacological Management of Infant and Young Child Procedural Pain." *Cochrane Database of Systematic Reviews*, vol. 2015, no. 12, December 2015, CD006275. Doi:10.1002/14651858.CD006275.pub3.
- [20] De Lima, J. and K.B. Carmo. "Practical Pain Management in the Neonate." *Best Practice & Research Clinical Anaesthesiology*, vol. 24, no. 3, 2010, pp. 291-307. Doi:10.1016/j.bpa.2010.04.001.
- [21] Committee on Fetus and Newborn and Section on Anesthesiology and Pain Medicine. "Prevention and Management of Procedural Pain in the Neonate: An Update." *Pediatrics*, vol. 137, no. 2, 2016, e20154271. Doi:10.1542/peds.2015-4271.
- [22] Johnston, C. *et al.* "Skin-to-Skin Care for Procedural Pain in Neonates." *Cochrane Database of Systematic Reviews*, vol. 2, February 2017, CD008435. Doi:10.1002/14651858.CD008435.pub3.
- [23] da Motta, G.C. and M.L. da Cunha. "Prevention and Non-Pharmacological Management of Pain in Newborns." *Revista Brasileira de Enfermagem*, vol. 68, no. 1, 2015, pp. 123-135. Doi:10.1590/0034-7167.2015680118p.
- [24] Liaw, J.J. *et al.* "Non-Nutritive Sucking and Facilitated Tucking Relieve Preterm Infant Pain During Heel-Stick Procedures: A Prospective, Randomised Controlled Crossover Trial." *International Journal of Nursing Studies*, vol. 49, no. 3, 2012, pp. 300-309. Doi:10.1016/j.ijnurstu.2011.09.017.
- [25] Slater, R. *et al.* "Oral Sucrose as an Analgesic Drug for Procedural Pain in Newborn Infants: A Randomised Controlled Trial." *The Lancet*, vol. 376, no. 9748, 2010, pp. 1225-1232. Doi:10.1016/S0140-6736(10)61303-7.
- [26] Stevens, B. *et al.* "Sucrose for Analgesia in Newborn Infants Undergoing Painful Procedures." *Cochrane Database of Systematic Reviews*, vol. 7, July 2016, CD001069. Doi:10.1002/14651858.CD001069.pub5.
- [27] Choi, J.C. *et al.* "Brain Mechanisms of Pain Relief by Transcutaneous Electrical Nerve Stimulation: A Functional Magnetic Resonance Imaging Study." *European Journal of Pain*, vol. 20, no. 1, 2016, pp. 92-105. Doi:10.1002/ejp.696.
- [28] Bellieni, C.V. *et al.* "Sensorial Saturation: An Effective Analgesic Tool for Heel-Prick in Preterm Infants: A Prospective Randomized Trial." *Biology of the Neonate*, vol. 80, no. 1, 2001, pp. 15-18. Doi:10.1159/000047113.
- [29] Mitchell, A.J. *et al.* "Does Noninvasive Electrical Stimulation of Acupuncture Points Reduce Heelstick Pain in Neonates?" *Acta Paediatrica*, vol. 105, no. 12, 2016, pp. 1434-1439. Doi:10.1111/apa.13581.
- [30] Kahraman, A. *et al.* "The Effects of Auditory Interventions on Pain and Comfort in Premature Newborns in the Neonatal Intensive Care Unit: A Randomised Controlled Trial." *Intensive and Critical Care Nursing*, vol. 61, 2020, 102904. Doi:10.1016/j.iccn.2020.102904.
- [31] Kucukoglu, S. *et al.* "Effect of White Noise in Relieving Vaccination Pain in Premature Infants." *Pain Management Nursing*, vol. 17, no. 6, 2016, pp. 392-400. Doi:10.1016/j.pmn.2016.08.006.
- [32] Bueno, M. *et al.* "A Systematic Review and Meta-Analyses of Nonsucrose Sweet Solutions for Pain Relief in Neonates." *Pain Research & Management*, vol. 18, no. 3, 2013, pp. 153-161. Doi:10.1155/2013/956549.
- [33] Carbajal, R. *et al.* "Morphine Does Not Provide Adequate Analgesia for Acute Procedural Pain Among Preterm Neonates." *Pediatrics*, vol. 115, no. 6, 2005, pp. 1494-1500. Doi:10.1542/peds.2004-1425.
- [34] Cignacco, E. *et al.* "The Efficacy of Non-Pharmacological Interventions in the Management of Procedural Pain in Preterm and Term Neonates: A Systematic Literature Review." *European Journal of Pain*, vol. 11, no. 2, 2007, pp. 139-152. Doi:10.1016/j.ejpain.2006.02.010.
- [35] Ohlsson, A. and P.S. Shah. "Paracetamol (Acetaminophen) for Prevention or Treatment of Pain in Newborns." *Cochrane Database of Systematic Reviews*, vol. 1, January 2020, CD011219. Doi:10.1002/14651858.CD011219.pub4.
- [36] Slater, R. *et al.* "Premature Infants Display Increased Noxious-Evoked Neuronal Activity in the Brain Compared to Healthy Age-Matched Term-Born Infants." *NeuroImage*, vol. 52, no. 2, 2010, pp. 583-589.
- [37] Vinall, J. *et al.* "Invasive Procedures in Preterm Children: Brain and Cognitive Development at School Age." *Pediatrics*, vol. 133, no. 3, 2014, pp. 412-421.
- [38] Grunau, R.E. *et al.* "Neonatal Pain, Parenting Stress, and Interaction, in Relation to Cognitive and Motor Development at 8 and 18 Months in Preterm Infants." *Pain*, vol. 143, nos. 1-2, 2009, pp. 138-146.
- [39] Anand, K.J.S. *et al.* "Repetitive Neonatal Pain and Neurocognitive Abilities in Ex-Preterm Children." *Pain*, vol. 154, no. 10, 2013, pp. 1899-1901.
- [40] Synnes, A. *et al.* "Determinants of Developmental Outcomes in a Very Preterm Canadian Cohort." *Archives of Disease in Childhood-Fetal and Neonatal Edition*, vol. 102, 2017, pp. F235-F243.
- [41] Brummelte, S. *et al.* "Procedural Pain and Brain Development in Premature Newborns." *Annals of Neurology*, vol. 71, no. 3, 2012, pp. 385-396.
- [42] Canbulat Şahiner, N. and A.S. Türkmen. "The Effect of Distraction Cards on Reducing Pain and Anxiety During Intramuscular Injection in Children." *Worldviews on Evidence-Based Nursing*, vol. 16, no. 3, June 2019, pp. 230-235.
- [43] Taddio, A. *et al.* "Physical Interventions and Injection Techniques for Reducing Injection Pain During Routine Childhood Immunizations: Systematic Review of Randomized Controlled Trials and Quasi-Randomized Controlled Trials." *Clinical Therapeutics*, vol. 31, January 2009, pp. S48-S76.
- [44] Yilmaz, G. and D.K. Alemdar. "Using Buzzy, ShotBlocker, and Bubble Blowing in a Pediatric Emergency Department to Reduce the Pain and Fear Caused by Intramuscular Injection: A Randomized Controlled Trial." *Journal of Emergency Nursing*, vol. 45, no. 5, September 2019, pp. 502-511.
- [45] Addab, S. *The Feasibility, Clinical Utility, Tolerability and Initial Clinical Efficacy of Virtual Reality Distraction with Children Undergoing Medical Procedures at a Specialized Pediatric Orthopedic Hospital*. McGill University (Canada), 2020.

- [46] Golmakani, S. *et al.* "Non-Pharmacological Techniques to Control Pain and Anxiety During Medical Procedures in Children Under 15 Years: A Systematic Review." *Journal of Research in Health and Medical Sciences*, vol. 1, no. 5, March 2023, pp. 69-81.
- [47] Melzack, R. and P.D. Wall. "Pain Mechanisms: A New Theory—A Gate Control System Modulates Sensory Input from the Skin Before It Evokes Pain Perception and Response." *Science*, vol. 150, no. 3699, November 1965, pp. 971-979.
- [48] Canbulat Şahiner, N. and A.S. Türkmen. "The Effect of Distraction Cards on Reducing Pain and Anxiety During Intramuscular Injection in Children." *Worldviews on Evidence-Based Nursing*, vol. 16, no. 3, June 2019, pp. 230-235.
- [49] Czub, M. *et al.* "Virtual Reality Distraction for Needle-Related Pain and Distress in Children: A Multicenter Randomized Controlled Trial." *Cyberpsychology, Behavior, and Social Networking*, vol. 27, no. 6, June 2024, pp. 409-419.
- [50] Inal, S. and M. Kelleci. "Relief of Pain During Blood Specimen Collection in Pediatric Patients." *MCN: The American Journal of Maternal/Child Nursing*, vol. 37, no. 5, September 2012, pp. 339-345.
- [51] Northington, L. "Society of Pediatric Nurses: A Year in Review." *Journal of Pediatric Nursing: Nursing Care of Children and Families*, vol. 56, January 2021, pp. 103-104.
- [52] Prabhakar, A.R. *et al.* "A Comparison Between Audio and Audiovisual Distraction Techniques in Managing Anxious Pediatric Dental Patients." *Journal of the Indian Society of Pedodontics and Preventive Dentistry*, vol. 25, no. 4, October 2007, pp. 177-182.
- [53] Felemban, O.M. *et al.* "Effect of Virtual Reality Distraction on Pain and Anxiety During Infiltration Anesthesia in Pediatric Patients: A Randomized Clinical Trial." *BMC Oral Health*, vol. 21, no. 1, June 2021, 321.
- [54] Simpson, K.R. and G.E. Knox. "Fundal Pressure During the Second Stage of Labor: Clinical Perspectives and Risk Management Issues." *MCN: The American Journal of Maternal/Child Nursing*, vol. 26, no. 2, March 2001, pp. 64-71.
- [55] Chambers, C.T. *et al.* "The Impact of Maternal Behavior on Children's Pain Experiences: An Experimental Analysis." *Journal of Pediatric Psychology*, vol. 27, no. 3, April 2002, pp. 293-301.
- [56] Blount, R.L. *et al.* "Management of Pediatric Pain and Distress Due to Medical Procedures." *Handbook of Pediatric Psychology*, Fourth Edition, Edited by Roberts, Michael C. and Ric G. Steele, New York, Guilford Publications, 2009, pp. 171-188.
https://www.google.com.pk/books/edition/Handbook_of_Pediatric_Psychology_Fourth/NUhJR1Hk9l4C?hl=en&gbpv=0.
- [57] Schwebel, D.C. *et al.* "Unintentional Child Poisoning Risk: A Review of Causal Factors and Prevention Studies." *Children's Health Care*, vol. 46, no. 2, April 2017, pp. 109-130.
- [58] Birnie, K.A.. "Psychological Interventions for Needle-Related Procedural Pain and Distress in Children and Adolescents." *Cochrane Database of Systematic Reviews*, vol. 10, 2018.
- [59] McMurtry, C.M. *et al.* "When 'Don't Worry' Communicates Fear: Children's Perceptions of Parental Reassurance and Distraction During a Painful Medical Procedure." *Pain*, vol. 150, no. 1, July 2010, pp. 52-58.
- [60] Karlsson, K. *et al.* "Nurses' Perspectives on Supporting Children During Needle-Related Medical Procedures." *International Journal of Qualitative Studies on Health and Well-Being*, vol. 9, no. 1, 2014, 23063.
- [61] Smith, W. "Concept Analysis of Family-Centered Care of Hospitalized Pediatric Patients." *Journal of Pediatric Nursing*, vol. 42, September 2018, pp. 57-64.
- [62] Nilsson, S. *et al.* "The Use of Virtual Reality for Needle-Related Procedural Pain and Distress in Children and Adolescents in a Pediatric Oncology Unit." *European Journal of Oncology Nursing*, vol. 13, no. 2, 2009, pp. 102-109. Doi:10.1016/j.ejon.2009.01.003.
- [63] Koch, A. *et al.* "Multiple Roles of Parental Caregivers of Children with Complex Life-Threatening Conditions: A Qualitative Descriptive Analysis." *Journal of Pediatric Nursing*, vol. 61, November 2021, pp. 67-74.
- [64] Hosseini, S.J. *et al.* "Effect of Acupressure on Venous Access Procedural Pain in Children: A Systematic Review and Meta-Analysis." *Complementary Therapies in Medicine*, July 2025, 103219.
- [65] Jafarzadeh, M. *et al.* "Effect of Aromatherapy with Orange Essential Oil on Salivary Cortisol and Pulse Rate in Children During Dental Treatment: A Randomized Controlled Clinical Trial." *Advanced Biomedical Research*, vol. 2, no. 1, January 2013, 10.
- [66] Birnie, K.A. *et al.* "Psychological Interventions for Needle-Related Procedural Pain and Distress in Children and Adolescents." *Cochrane Database of Systematic Reviews*, vol. 10, 2018.
- [67] Schaa, K.L. *et al.* "Genetic Counselors' Implicit Racial Attitudes and Their Relationship to Communication." *Health Psychology*, vol. 34, no. 2, February 2015, pp. 111-118.